REMARKS

Upon entry of the amendments herein, claims 14-19 remain pending in the application. Claims 9-13 have been cancelled, and claims 14 and 17-19 have been amended.

Applicants note, in the first place, that the Examiner has prefaced his rejections with the statement "The abbreviation **IBD** is used hereinbelow to denote 'irritable bowel syndrome'." The Examiner apparently believes that IBS (**irritable** bowel **syndrome**), which is the condition to which the present invention is directed, and IBD (**inflammatory** bowel **disease**) are one and the same. However, this is certainly not the case, and the Examiner's assessments, all drawn in connection with IBD, are inappropriate to the patentability analysis of the present case. Applicants are providing for the Examiner's enlightenment a copy of a public article from the Crohn's and Colitis Foundation of America (CCFA) website entitled "IBS and IBD: Two Very Different Disorders." This reference is being made of record via an Information Disclosure Statement, also being submitted on today's date.

Claims 9 and 13-19 stand rejected under 35 U.S.C. §112, first paragraph as not being enabled by the specification. Applicants will address this issue only in terms of claims 14-19, as claims 9 and 13 have been cancelled.

The Examiner acknowledges Applicants' showing that compounds of the present invention are effective in reducing the visceromotor response (VMR) to colorectal distension (CRD), but asserts that Applicants have made no attempt to relate this finding to the claimed invention. The Examiner goes on to state, erroneously: "The claimed invention is treatment of IBD." The Examiner further asserts: "Applicants have made no assertion (or provided any evidence) that the underlying inflammation is affected one way or another by the compounds."

Again, the claimed invention relates to the treatment of IBS and, as made abundantly clear by the enclosed CCFA article, IBS is not the same as IBD. Furthermore, as the CCFA article clearly teaches, IBD is a disease and is associated with inflammation and permanent damage to the intestines. On the other hand, IBS is classified as a **functional** gastrointestinal disorder, not a disease but a syndrome, defined as a group of symptoms.

The Examiner does not believe that one of the skill in the art would find the CRD model suitable or that said artisan would see any connection between attenuation of VMR elicited by CRD, on the one hand, and beneficial treatment of IBD on the other. Again, for starters, the Examiner should have conducted this

analysis in the context of treatment of IBS, a condition much different from IBD.

As taught in the CCFA article, it is currently believed that IBS is caused by a disturbance in the way the brain and gut interact. As disclosed in the specification (see page 2, lines 6-10), the hypersensitive state associated with **functional** bowel disorders such as IBS may occur as a result of excessive receptor activation and, thus, compounds such as those of the present invention may be advantageous, as they can only block the receptor when it is in an activated state. Still further, as disclosed in the present specification, the data presented in the application (see both Examples) indicate that the activity at the peripheral NMDA receptors plays a role in modulating responses to CRD. These are considerations that would not apply to an approach to treatment of IBD.

The Examiner certainly would not argue against the idea that colorectal distension produces a visceromotor response. As taught in the CCFA article, one of the symptoms of IBS is abdominal distension (which would include colorectal distension). One of skill in the art would thus certainly find the connection between attenuation of VMR and alleviation of symptoms associated with IBS credible.

Applicants further wish to point out that CRD constitutes a stimulus method that is employed as a means of screening for compounds that can be used for treating IBS. The Examiner is invited to consider more carefully Example 1 of the present application.

The Examiner has focused on the CRD/VMR model (Example 1), to the exclusion of the model (testing pelvic afferent nerve activity) described in Example 2 of the specification. The results obtained from this second model show reduction of pelvic nerve activity elicited by CRD and thus also provide support for the assertion of efficacy of the recited compounds in the claimed method of treatment.

It should be clear, then, that the models employed and the data obtained therefrom provide a perfectly adequate connection such that one of skill in the art would find it credible that the demonstrated effects of the compounds according to the instant invention reflect the usefulness of the compounds in the treatment of IBS. No undue experimentation is required to make this connection, and the rejection must be withdrawn.

Claims 9 and 13-19 also stand rejected under 35 U.S.C. §112, second paragraph as being indefinite "as to the manifestations of a successful treatment." Claims 9 and 13 have been cancelled but claims 14-19 remain pending.

As with the previous rejection, the Examiner's analysis in the context of treatment of IBD is inappropriate to the present case. Contrary to the Examiner's assessment, a successful method of treating irritable bowel syndrome would not be expected to result in mitigation of inflammation. Thus, the fact that Applicants' "measure of success" is not connected with reduction of inflammation is of no moment. Furthermore, as made clear in the preceding arguments, the Examiner's statement that Applicants' measure of success has nothing to do with the well being of the patient is untenable. One of skill in the art would most certainly find it credible that the instant method of treatment would make an IBS patient feel better, due both to attenuation of VMR and to reduction of pelvic nerve activity elicited by CRD, effects of the recited compounds that are amply demonstrated by the data presented in Examples 1 and 2.

Even if the Examiner's reasoning were correct, and it is not, the requirement that the claims literally recite the "manifestations of a successful treatment" is unwarranted. A standard, acceptable method-of-treatment claim may simply recite the administration of an active agent in an amount effective to treat a given condition. It would be accepted that such treatment would alleviate the symptoms, whatever they might be, of the recited condition(s), based on the connection(s) taught

in the specification and the support provided for the connection(s). The present claims meet the criteria for patentability under 35 U.S.C. §112, second paragraph.

Applicants note the Examiner's suggestion of an amended claim that would possibly overcome the rejection. Again, Applicants have adequately supported a connection between NMDA antagonism and amelioration of symptoms of IBS, and it is not necessary that the mechanism or connection per se be recited in the claims. Furthermore, as seen by considering both specification Examples, it would not be appropriate to limit the claims solely to a mechanism involving CRD-induced VMR. Applicants emphatically maintain that the claims need not be amended in this way to meet the criteria for patentability.

Claim 17 has further been rejected as indefinite on the allegation that the compounds recited therein do not fall within the genus defined in claim 14, from which it depends. Claim 17 has been amended to make it independent, rendering moot the rejection.

Claims 9 and 13 stand rejected under 35 U.S.C. §103 as being obvious over the combination of the references of Alam and Martin. The cancellation of these claims renders moot their rejection.

Claims 9 and 14 also stand rejected under 35 U.S.C. §103 as being obvious over U.S. Patent No. 6,048,543 to Schneider et al. Claim 9 has been cancelled and 14, in amended form, remains pending. The Examiner cites the Schneider teaching that glycine can be used to treat inflammatory bowel diseases and maintains that one of the ordinary skill would regard IBD as an inflammatory bowel disease and further would regard glycine as a metabolite of the compounds of formula I in claim 14.

Again, however, the condition to be treated according to the present invention, IBS, is not an inflammatory bowel disease. Applicants note that the Schneider passage cited by the Examiner teaches treatment of "inflammatory bowel diseases such as ulcerative colitis and Crohn's disease." The confluence of this teaching and the teaching in the CCFA article that IBD encompasses such diseases, but that IBS does not, further clarifies the untenability of the Examiner's position. In summary, as is generally well known in the art, the etiologies and manifestations of IBS are much different from those of IBD. Thus, whether or not the Examiner's assertion that one of skill in the art would regard glycine as a metabolite of compounds of claim 14 is true, the skilled artisan would have no expectation that glycine would be useful in the treatment of IBS. The cited

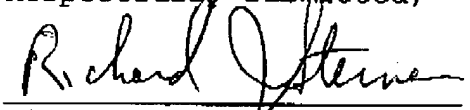
disclosure of the Schneider reference cannot be taken as teaching or suggesting the present invention.

The stated grounds for rejections have all either been fully addressed or overcome by the amendments presented and Applicants' showing herein. The application is in condition for allowance; reconsideration and allowance of the application with pending claims 14-19 are respectfully requested. Should any other matters require attention prior to allowance, it is requested that the Examiner contact the undersigned.

The Commissioner is hereby authorized to charge any additional fees which may be due for any reason to Deposit Account No. 23-1703.

Dated: February 21, 2006

Respectfully submitted,



Richard J. Sterner
Reg. No. 35,372

Customer No. 007470
(212)819-8200

Agent's Direct line:
(212) 819-8783